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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,361	08/25/2003	Mark L. Weiss	KSURF-08401	2222

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/647,361	WEISS ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,12-14,16-21,32-35 and 41-43* is/are pending in the application.

4a) Of the above claim(s) *14,32 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 12, 13, 16-21, 34-35, 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment and Response, filed 10/30/08 has been entered. Claims 1, 3, 12, 16-21, 34, 35, 41-43 are amended; claims 14, 32 and 33 are withdrawn; claims 1, 3, 12, 13, 16-21, 34-35, 41-43 are under current examination.

The Mitchell Declaration, filed 10/30/08 has been considered.

Election/Restrictions

Claims 14, 32 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/14/06.

Applicant's election without traverse of Group I (claims 1-3, 12, 13, 16-22, 34, 35 and 41-43) in the reply filed on 8/14/06 is acknowledged.

Color Drawings

Applicants have replaced the color drawings with black and white drawings. These drawings are accepted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 12, 13, 16-21, 34-35, 41-43 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such

a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record advanced in the prior Office action.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments & Mitchell Declaration. Applicants argue that the claims, as amended, are enabled. Applicants argue that the specification has provided uses for heterogeneous cell populations that contain UCMS cells and point to Example 1 which teaches that the population of cells can be used to produce neural stem cells and neuronal cells; Example 8, which shows that populations of cells comprising UCMS cells can be transplanted into the brains of rats without stimulating an immune response, survive for many weeks and differentiate into neural cells; Example 9, which demonstrate that the population of cells contain human UCMS cells that can be transplanted into the brains of rats that model Parkinson's disease and that the transplanted cells have a substantial benefit on the behavior of the rats. See p. 9, 1st ¶ of the Response

In the prior rejection the Examiner discussed that the specification teaches the expression of various markers, such as c-kit and alkaline phosphatase, but it unclear if these cells were found in a heterogeneous population of cells, and it is unclear if the cells/colonies expressed these markers simultaneously. Applicants argue that the amendment of the claims now render this aspect of the rejection moot because the claims are directed to populations of cells comprising UCMS cells. Additionally, the Mitchell Declaration teaches that these process steps result in a population of cells that is distinguishable from Wharton's jelly cells. In particular,

the Mitchell Declaration describes in detail how the cells produced by the claimed process provide a cell population with distinct characteristics, and thus, the specification teaches how make and use the claimed cell populations. See pages 9-10 of the Response.

The Mitchell Declaration is generally directed to comparing cells of the art (Purchio) and the instantly claimed cells. The Examiner addresses these arguments in further detail below. The Declaration discusses various cell surface markers that are expressed in the UCMS cells and that the cell populations obtained by the instant specification are produced by the process of enzymatic dispersion and passaging, which is substantially different from the cell population in unprocessed Wharton's jelly. See #7 of the Declaration. The Mitchell Declaration teaches that stripping the amniotic covering or vesicles, without extreme care would essentially eliminate the UCMS stem cells from Wharton's jelly prior to its culturing (pp. 5-6). The Mitchell Declaration points to Examples 8-9 as an example of how to use the heterogeneous population of cells that are instantly claimed. The Declaration states that regarding the particular identifying characteristics of a UCMS cell, a person of ordinary skill in the art would recognize that the specification teaches a method to obtain the populations of cells used in the working examples 7-8, and the post-filing art of Jomura and Hirko which show that the cells have a significant protective effect in whole-brain ischemia. See pages 10-12 of the Declaration.

Response To Arguments. These arguments have been fully considered, but are not persuasive. The Examiner maintains that the specification does not provide guidance for an enabled use of heterogeneous cell populations. The specification provides a specific definition of a UCMS cell, which includes that this cell is capable of unlimited mitotic divisions and a UCMS cell can produce cells from any of the three germ layers or germ cells (see p. 19, lines 3-10). The specification provides guidance with regard to isolation of a heterogeneous population of cells, which

includes UCMS cells. As stated previously, it is unclear from the specification if the umbilical cord matrix stem cells in the resultant culture could be identified by being negative for CD34/CD45, positive for telomerase activity, can be expanded *in vitro* and maintained in culture through repeated passages, because if the resultant culture contained different cell types, it is unclear which cell type has which (or all) of the claimed characteristics. Therefore, a heterogeneous population of cells, which includes many different cell types, is used in Examples 8-9. It is unclear from the working examples if the effects that are reported (*i.e.*, implantation of UCMS cells in Example 8, or transplantation of the population of cells into a Parkinsonian rat model) are produced by the UCMS cells, or by other cells in the population. The Examiner maintains that although the specification teaches expression of various markers, such as c-kit or alkaline phosphatase, however, it appears that these cells were found in a heterogeneous population of cells, and it is unclear if these cells/colonies expressed both markers simultaneously. Thus, given it is unclear if one particular cell, or a population of mixed cells expressed the claimed characteristics, it would have required one of skill to practice undue experimentation in order to determine which cell(s) would express the appropriate markers that would sufficiently arrive at obtaining a UCMS cell.

Given that the specification fails to provide specific guidance for the heterogeneous population of cells, and particularly, with regard to the markers and phenotype of the UCMS cells, it would have required one of skill in the art undue experimentation to determine the characteristics specifically attributed to the UCMS cells, and then further undue experimentation, to determine if the *in vivo* results in the specification are an effect of transplantation of a heterogeneous population of cells that contain UCMS cells is a result of UCMS cells or other cells found in the heterogeneous population of cells.

As stated previously, the specification fails to provide guidance for UCMS cells as a particular cell type – and only provides guidance for this cell in a

composition including other cells. Although the amendment to the claims no longer requires only UCMS cells, and encompasses a heterogeneous population of cells, the breadth of the claimed invention is not enabled. Given that the particular markers and characteristics that are instantly claimed, as well as taught in the specification, are expressed in various cell types, it would have required one of skill in the art to practice undue experimentation to determine what type(s) of cells are encompassed by UCMS cells, because the markers that are identified to be expressed by the claimed cells are expressed in other cell types.

Accordingly, the rejection is maintained.

Written Description

Claims 1, 3, 12, 13, 16-21, 34-35, 41-43 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the specification and examples demonstrate that Applicants had possession of a population of cells comprising UCMS cells as presently claimed.

The Declaration states that regarding the particular identifying characteristics of a UCMS cell, a person of ordinary skill in the art would recognize that the specification teaches a method to obtain the populations of cells used in the working examples 7-8, and the post-filing art of Jomura and Hirko which show that the cells have a significant protective effect in whole-brain ischemia. See pages 10-12 of the Declaration.

These arguments are not persuasive. The amended claims are directed to a population of cells that comprise UCMS cells. However, the claims require UCMS cells. There is no guidance in the working examples with regard to the particular,

identifying characteristics of a UCMS cell, only to a population of cells which comprise UCMS cells (*i.e.*, a heterogeneous population of cells). The working examples fail to provide specific characteristics that would be present in a UCMS cell because the working examples only discuss these characteristics in a heterogeneous population of cells, wherein different cells could express the markers (or absence of markers) and other characteristics required by the claims. That is, the specification provides no specific, identifying features of UCMS cells, other than features that are present in a heterogeneous population of cells. It is unclear if the characteristics described in the specification are attributable to UCMS cells, or other cells present in the culture.

Accordingly, the as-filed disclosure fails to provide a written description for the claimed UCMS cells, and as such, there is no indication that Applicants had possession of the claimed invention. The claims have now been amended to recite "enriched" (see claim 3, for example). However, the term "enriched" fails to provide a reduction to practice with regard to the characteristics of a UCMS cell. In particular, the term "enriched" encompasses any type of enrichment, and is a relative term. It is maintained that the specification fails to provide sufficient written description for the stem cells, as instantly claimed. Accordingly, the as-filed disclosure fails to provide a written description for the claimed UCMS cells, and as such, there is no indication that Applicants had possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 34, 35 stand rejected under 35 U.S.C. 102(b) as being anticipated by Purchio *et al.*(US Pat. No. 5,919,702, July 6, 1999).

Claim interpretation: The claims are interpreted as follows: the claims are directed to a population of cells enriched for umbilical cord matrix stem cells isolated from an umbilical cord matrix source of stem cells wherein the umbilical cord matrix is enyzmatically dispersed to provide a fraction of cells comprising UCMS cells, and exposing the enzymatically dispersed cells to conditions suitable for stem cell proliferation and passaging the UCMS cells to remove non-adherent cells thus selecting for a fraction of cell enriched for UCMS cells, wherein the UCMS cells are negative for CD34, CD45, positive for telomerase activity, can be expanded in vitro and be maintained in culture through repeated passages. Further embodiments are directed to a population of cells containing human UCMS cells isolated by the method above. With regard to the amendment to the claims which recites that the cells are "enriched" for UCMS cells, the term "enriched" fails to provide patentable weight to the claims because the term "enriched" is a relative term. For example, any cell population which would reasonably contain any UCMS cells would be "enriched" for these cells, when compared to a cell population that does not contain UCMS cells.

Applicants' Arguments & Mitchell Declaration. Applicants argue that the Purchio document does not anticipate the claims because Purchio have isolated chrondrogenic progenitor cells, or pre-chondrocytes from Wharton's jelly, and reported the isolation of cells from human umbilical cord Wharton's jelly by removal of blood, blood vessels and the amnion lining of the umbilical cord, followed by incubating the tissue under conditions to allow migration of pre-chondrocytes to migrate from the Wharton's jelly explants. Applicants argue that the method does not distinguish desired cells from different cell types present in Wharton's Jelly, nor those present in the entirety of the umbilical cord matrix, but relies upon migration

of the cells. Applicants submit that the current claims render this rejection moot because the composition claims have been amended to specify that a population of cells is isolated by a three-step process, and that the current claim isolates cells that are not contained within the Purchio method, because they rely upon migration of cells from Wharton's jelly, whereas the claimed method enzymatically treats the entire matrix, and therefore cells are isolated that cannot be isolated from the Purchio method. In particular, Applicants argue that the Office has not established any reasonable basis that the cells described by the Purchio reference are the cell populations or contain the cell population as made by the instant process, and that office has not provided any basis to show that the cells described by Purchio are those recited in the instant claims. Applicants point to the Mitchell Declaration and state that this clearly establishes that Purchio's cells are not and supports the contention that the complex structure of the umbilical cord would make it such that the methodology of isolation from the umbilical cord would, in fact, result in different cells. See pages 12-13 of the Response.

Mitchell Declaration. The Mitchell Declaration discusses several points:

1. The comparison of the Weiss-UCMS cells and Purchio pre-chondryocyte cell surface expression markers (#6, Tables 1-2) and states that there are distinct differences between the cell populations taught by Purchio and that of the instant invention.

2. Purchio's lack of discussion of the complex structure of Wharton's jelly, namely in that there are 3 distinct zones of stromal cells and matrix that can be identified in the umbilical cord: the subamniotic layer, Wharton's jelly and the media and adventitia surround the vessels. See #8.

3. Investigation of proteins expressed by UCMS cells *in situ* found that they are expressed by cells in specific regions of the umbilical cord. In particular Oct-4 expression and vimentin expressing cells are confined to specific regions, near the vessels and beneath the amnion, and that the major portion of Wharton's jelly is

not populated with these cell types, and that the stripping of the amniotic covering or vessels, described by Purchio without extreme care would essentially eliminate these stem cells from the Wharton's jelly prior to its culturing. Thus, the method of Purchio, which strips the amnion and vessels would lose the vimentin positive cells that are found in only specific regions of the cord matrix. See p. 7.

4. Purchio teach sections of Wharton's jelly are removed from the umbilical cord and cultured, and that this process would result in substantially different cell populations than that which is produced by the claimed methods. The Mitchell Declaration discusses the difference between the pre-chondryocytes isolated by the Purchio method and the instant UCMS cells with regard to marker expression, morphology and differentiation capability. See pages 7-9 of the Declaration.

Response to Arguments. These arguments have been fully considered, but are not persuasive. The arguments by Applicants, as well as the Mitchell Declaration appear to argue that the method of isolation of the UCMS cells of the instant invention provides a patentable distinction between the claimed population of cells, and that which is produced by Purchio. Preliminarily, certain embodiments are directed to "enriched" populations of UCMS cells, however, as discussed above, this term does not provide patentable weight. Broadly interpreted, the claims encompass any population of cells that has any amount of UCMS cells. Additionally, the Examiner notes that the instant specification teaches the following:

1. To isolate the stem cells of the claimed invention, an umbilical cord, or section thereof can be used to collect Wharton's jelly. "Wharton's Jelly is collected from the umbilical cord under sterile conditions by an appropriate method known in the art. For example, the cord is cut transversely by a scalpel...." See p. 21, lines 28-30. In particular, "***The blood vessels of the umbilical cord (two veins and an artery" are dissected away, for example with sterile forceps and dissecting scissors***

... The umbilical cord may then be cut into smaller sections, such as 2-3 mm^3 for culturing. See p. 22, lines 2-6, emphasis added. Although the specification teaches that any known alternative method may be used (such as enzymatic dissection, after the initial isolation of the umbilical cord, see p. 22, lines 8-11, for example; or by fractionation and enzymatic treatment; p. 23, lines 7+), the specification clearly teaches that UCMS cells can be isolated by methods known in the art, which are the same as the methods taught by Purchio.

2. Additionally the specification teaches that, regarding the UCMS cells, "The cells are derived from Wharton's jelly matrix rather than cord blood because umbilical vessels are stripped from the cord before explant preparation and the cells are negative for markers of the hematopoietic lineage such as CD34 and CD45." See p. 39, lines 21-24.

Therefore, the Declaration and Applicants' arguments are not persuasive because the claims do not require any degree of enrichment, and in view of the specification's teaching that the stripping of umbilical vessels would still result in the production of UCMS cells, the Examiner maintains that there would a reasonable expectation that the methods of Purchio, who discuss isolating, collecting and culturing Wharton's jelly would contain some UCMS cells.

With regard to Applicants' comparison between Purchio's pre-chondrocytes and the instantly claimed cells, the Examiner notes that this is not within the scope of the rejection. The rejection is based upon the claims, which broadly encompass any population of cells that contain UCMS cells. Purchio teaches the isolation and culture of Wharton's jelly, which also contains UCMS cells. Therefore, given that Purchio teaches cells that are isolated from the same source, and produced by methods that are taught by the specification, the Wharton's jelly culture that is taught by Purchio anticipates the instant claims.

Purchio teach cultures of Wharton's jelly (see col. 10-11, #5.1) that can be cultured and expanded. Accordingly, because Purchio teach a culture of cells from

the same source as the instantly claimed cell compositions, Purchio's culture would inherently contain the cell compositions and cultures as instantly claimed. Therefore, any properties claimed for the cells would also be necessarily present. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632